

SPECIALTY GUIDELINE MANAGEMENT

AVASTIN (bevacizumab) MVASI (bevacizumab-awwb) ZIRABEV (bevacizumab-bvzr)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic colorectal cancer (mCRC)
 - a. Avastin, Mvasi, or Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
 - b. Avastin, Mvasi, or Zirabev, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab-containing regimen.
2. First-line non-squamous non-small cell lung cancer (NSCLC)
Avastin, Mvasi, or Zirabev, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer.
3. Recurrent glioblastoma (RGM)
Avastin, Mvasi, or Zirabev, is indicated for the treatment of recurrent glioblastoma in adults.
4. Metastatic renal cell carcinoma (mRCC)
Avastin, Mvasi, or Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.
5. Persistent, recurrent, or metastatic cervical cancer
Avastin, Mvasi, or Zirabev, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.
6. Epithelial ovarian, fallopian tube, or primary peritoneal cancer
 - a. Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
 - b. Avastin, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
 - c. Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

B. Compendial Uses

1. Breast cancer for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative disease
2. Central nervous system (CNS) cancers
 - a. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
 - b. Intracranial and spinal ependymoma (excluding subependymoma)
 - c. Anaplastic gliomas
 - d. Medulloblastoma

- e. Primary central nervous system lymphoma
- f. Meningiomas
- g. Limited and extensive brain metastases
- h. Leptomeningeal metastases
- i. Metastatic spine tumors
- 3. Malignant pleural mesothelioma
- 4. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
 - a. Carcinosarcoma (malignant mixed Müllerian tumors)
 - b. Clear cell carcinoma
 - c. Mucinous carcinoma
 - d. Grade 1 endometrioid carcinoma
 - e. Low-grade serous carcinoma
 - f. Ovarian borderline epithelial tumors (low malignant potential) with invasive implants
 - g. Malignant sex cord-stromal tumors
- 5. Soft tissue sarcoma
 - a. Angiosarcoma
 - b. Solitary fibrous tumor/Hemangiopericytoma
- 6. AIDS-related Kaposi sarcoma
- 7. Uterine/Endometrial cancer
- 8. Vulvar cancer
- 9. Peritoneal mesothelioma
- 10. Pericardial mesothelioma
- 11. Tunica vaginalis testis mesothelioma
- 12. Small bowel adenocarcinoma
- 13. Appendiceal carcinoma
- 14. Anal adenocarcinoma
- 15. Ophthalmic disorders
 - a. Diabetic macular edema
 - b. Neovascular (wet) age-related macular degeneration (AMD)
 - c. Macular edema following retinal vein occlusion (RVO)
 - d. Proliferative diabetic retinopathy
 - e. Choroidal neovascularization (CNV)
 - f. Neovascular glaucoma; adjunct
 - g. Retinopathy of prematurity
 - h. Polypoidal choroidal vasculopathy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Ophthalmic disorders

Authorization of 6 months may be granted for treatment of the following retinal disorders:

- 1. Diabetic macular edema
- 2. Neovascular (wet) age-related macular degeneration
- 3. Macular edema following retinal vein occlusion
- 4. Proliferative diabetic retinopathy
- 5. Choroidal neovascularization (including myopic choroidal neovascularization, angioid streaks, choroiditis [including choroiditis secondary to ocular histoplasmosis], idiopathic degenerative myopia, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum, and trauma)
- 6. Neovascular glaucoma
- 7. Retinopathy of prematurity
- 8. Polypoidal choroidal vasculopathy

B. Colorectal cancer (CRC)

Authorization of 12 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma.

C. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic non-squamous NSCLC.

D. CNS cancer

Authorization of 12 months may be granted for treatment of the following types of CNS cancer:

1. Glioblastoma
2. Intracranial and spinal ependymoma (excludes subependymoma)
3. Anaplastic gliomas
4. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
5. Medulloblastoma
6. Primary central nervous system lymphoma
7. Meningiomas
8. Limited and extensive brain metastases
9. Leptomeningeal metastases
10. Metastatic spine tumors

E. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer

Authorization of 12 months may be granted for treatment of the following types of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer:

1. Epithelial ovarian cancer, including:
 - i. Carcinosarcoma (malignant mixed Müllerian tumors)
 - ii. Clear cell carcinoma
 - iii. Mucinous carcinoma
 - iv. Grade 1 endometrioid carcinoma
 - v. Low-grade serous carcinoma
 - vi. Borderline epithelial tumors (low malignant potential) with invasive implants
 - vii. Malignant sex cord-stromal tumors
2. Fallopian tube cancer
3. Primary peritoneal cancer

F. Uterine/Endometrial cancer

Authorization of 12 months may be granted for treatment of progressive, advanced, or recurrent uterine cancer or endometrial cancer.

G. Cervical/Vaginal cancer

Authorization of 12 months may be granted for treatment of persistent, recurrent, or metastatic cervical or vaginal cancer.

H. Breast cancer

Authorization of 12 months may be granted for treatment of breast cancer.

I. Renal cell carcinoma

Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma.

J. Soft tissue sarcoma

Angiosarcoma

Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.

Solitary fibrous tumor/hemangiopericytoma

Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

K. Malignant pleural mesothelioma

Authorization of 12 months may be granted for treatment of malignant pleural mesothelioma, in combination with pemetrexed and either cisplatin or carboplatin, followed by single agent maintenance therapy.

L. AIDS-related Kaposi sarcoma

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma.

M. Vulvar cancer

Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic vulvar cancer.

N. Peritoneal mesothelioma

Authorization of 12 months may be granted for treatment of peritoneal mesothelioma.

O. Pericardial mesothelioma

Authorization of 12 months may be granted for treatment of pericardial mesothelioma.

P. Tunica vaginalis testis mesothelioma

Authorization of 12 months may be granted for treatment of tunica vaginalis testis mesothelioma.

III. CONTINUATION OF THERAPY

A. Ophthalmic disorders

For ophthalmic disorders, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

B. All other indications

For all other indications, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who are experiencing a clinical benefit to therapy or who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. Mvasi [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2019.
3. Zirabev [package insert]. New York, NY: Pfizer Inc.; June 2019.
4. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed January 7, 2020.
5. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com>. Accessed January 7, 2020.
6. Chan WM, Lai TY, Lui DT, et al. Intravitreal bevacizumab (Avastin) for myopic choroidal neovascularization: 1-year results of a prospective pilot study. *Br J Ophthalmol*. 2009;93(2):150-154.

7. Gupta B, Elagouz M, Sivaprasad S. Intravitreal bevacizumab for choroidal neovascularization secondary to causes other than age-related macular degeneration. *Eye*. 2010;24:203-213.
8. CATT Research Group, Martin DF, Maguire MG, et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med*. 2011;364(20):1897-1908.
9. Russo V, Barone A, Conte E, et al. Bevacizumab compared with macular laser grid photocoagulation for cystoid macular edema in branch retinal vein occlusion. *Retina*. 2009;29:511-5.
10. Michaelides M, Kaines A, Hamilton RD, et al. A prospective randomized trial of intravitreal bevacizumab or laser therapy in the management of diabetic macular edema (BOLT Study) 12-month data: report 2. *Ophthalmology*. 2010;117:1078-1086.
11. Mirshahi A, Roohipour R, Lashay A, et al. Bevacizumab-augmented retinal laser photocoagulation in proliferative diabetic retinopathy: a randomized double-masked clinical trial. *Eur J Ophthalmol*. 2008;18(2):263-269.
12. Yazdani S, Hendi K, Pakravan M, et al. Intravitreal bevacizumab for neovascular glaucoma: a randomized controlled trial. *J Glaucoma*. 2009;18(8):632-637.
13. Mintz-Hittner HA, Kennedy KA, Chuang AZ, et al. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. *N Engl J Med*. 2011;364(7):603-615.
14. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015>.
15. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2017. Available at: <https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017>.
16. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/retinal-vein-occlusions-ppp-2015>.
17. VanderVeen DK, Melia M, Yang MB, et al. Anti-vascular endothelial growth factor therapy in primary treatment of type 1 retinopathy of prematurity: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2017. May;124(5):619-633.
18. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed January 7, 2020.
19. Yong M, Zhou M, Deng G. Photodynamic therapy versus anti-vascular endothelial growth factor agents for polypoidal choroidal vasculopathy: A meta-analysis. *BMC Ophthalmol*. 2015;15:82.
20. Kim JH, Kim JW, Lee TG, Lew YJ. Treatment outcomes in eyes with polypoidal choroidal vasculopathy with poor baseline visual acuity. *J Ocul Pharmacol Ther*. 2015;31(4):241-247.
21. Oishi A. The evidence for the treatment of polypoidal choroidal vasculopathy. *Nippon Ganka Gakkai Zasshi*. 2015;119(11):781-786.
22. Chang YS, Kim JH, Kim KM, et al. Long-term outcomes of anti-vascular endothelial growth factor therapy for polypoidal choroidal vasculopathy. *J Ocul Pharmacol Ther*. 2016;32(4):219-224.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed January 7, 2020.
24. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed January 7, 2020.
25. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed January 7, 2020.
26. PDQ® Adult Treatment Editorial Board. PDQ Vaginal Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated November 15, 2019. Available at: <https://www.cancer.gov/types/vaginal/hp/vaginal-treatment-pdq>. Accessed January 8, 2020. [PMID: 26389242]

Reference number(s)
1891-A

27. PDQ® Adult Treatment Editorial Board. PDQ Cervical Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated December 12, 2019. Available at: <https://www.cancer.gov/types/cervical/hp/cervical-treatment-pdq>. Accessed January 8, 2020. [PMID: 26389493]